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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/667,191
Filing Date: September 15, 2003
Appellant(s): ZHENG ET AL.

Karen Canaan
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed August 21, 2008 appealing from the Office action mailed December 28, 2007.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

The copy of the appealed claims contained in the Appendix to the brief is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Wilton et al. "Snapback SSCP Analysis: Engineered Conformation Changes for the Rapid typing of Known Mutations" Human Mutation, vol. 11, (March 1, 1998), pp. 252-258.

The Stratagene Catalog. 1988, p. 39.

5,573,906	Bannwarth et al.	11-1996
US 2002/0028455	Laibinis et al.	3-2002

6,268,147 Beattie et al. 7-2001

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Interpretation

Claims 1-18 and 26-35 are product claims directed to primers and nucleic acid constructs. The claims include functional limitations and recitations of intended use that are dependent on the particular target nucleic acid sequence that the claimed primer is intended to copy or amplify. However, **no specific target sequences are specified.** Therefore, such functional limitations and recitations of intended use confer no structural limitations to the claimed primer, and will be given **no patentable weight.** As written, the claimed primer is anticipated by any prior art primer for which a target sequence exists **or could be synthesized** such that the functional limitations and intended uses recited in the claims are fulfilled. Only those limitations that impart **target-independent** structural limitations on the claimed primers will be considered. Additionally, any oligonucleotide with a 3' extendable end is a primer.

Claim Rejections - 35 USC § 112-Written Description

Claims 1-18 and 26-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

All claims are directed to isolated polynucleotides of one form or another which are complementary to, or substantially complementary to, or capable of being extended on an unspecified target sequence. Applicants have chosen to claim these polynucleotides not based on their chemical structure, but based on function. Since no particular sequence is specified, for either the target or the

primer, this creates an incredibly large genus of potential polynucleotides covered by the claims. The claims encompass any polynucleotide for which a target sequence exists *or could be synthesized.*

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed (See *Vas-Cath* at page 1117)." The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed (See *Vas-Cath* at page 1116)."

The skilled artisan cannot envision the detailed chemical structure of the encompassed nucleic acids. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. *See Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993), and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that 'the inventor invented the claimed invention.' Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (' [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.'). Thus, an applicant complies with the written description requirement 'by describing the invention, with all its claimed limitations, not that which makes it obvious,' and by using 'such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention.' Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

The written description requirement ensures that, "an applicant invented the subject matter which is claimed. Further, the written description requirement for a claimed genus may be satisfied *through a sufficient description of a representative number of species* by 1) *reduction to practice*; 2) *reduction to drawing*; or 3) *disclosure of relevant identifying characteristics (i.e., structure of other physical and/or chemical properties, functional characteristics coupled with a known or disclosed correlation between function and structure* (MPEP 2163 at II(A)(3)(a)(ii)).

With regard to a representative number of species, Applicants' disclosure contains no specific sequences of targets or primers and as written the claims encompass an incredibly large genus of potential polynucleotides covered by the claims. The claims encompass any polynucleotide for which a target sequence exists *or could be synthesized.*

Since no specific polynucleotide sequence or no specific template sequence is recited, Applicants have not described the sequence information required to define the genus of all primers that would provide the requisite functional limitations required by the claims.

Therefore, as Applicants have not adequately defined the genus in terms of the structure required to perform the function and have not adequately described the enormous number of potential primers falling within the genus claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 9, 12-14 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Wilton et al. (Human Mutation 1998, cited in the IDS).

With regard to claim 1, Wilton et al. teach a dual-purpose primer for amplifying a target nucleotide sequence in a target molecule, wherein the target molecule has a secondary structure forming region and further wherein the target nucleotide sequence contains a site of interest proximal to or contained within the secondary structure forming region, wherein the primer comprises:

(a) a primer sequence complementary to a segment of the target nucleotide sequence other than the secondary structure forming region (see p. 253, Table 1 and col. 2 lines 10-17 and Figure 1, where

Wilton et al. clearly teach a primer sequence which is complementary to a target nucleotide sequence which is the only structural limitation recited, see ***Claim Interpretation*** above); and

(b) a blocking sequence substantially complementary to a segment of the secondary structure forming region wherein the blocking sequence disrupts formation of the unwanted secondary structure in an amplicon thereby enabling detection and amplification of the site of interest (see p. 253, Table 1 and col. 2 lines 10-17 and Figure 1, where Wilton et al. clearly teach a primer sequence which is complementary to a target nucleotide sequence which is the only structural limitation recited. The recitation of "blocking sequence substantially complementary to a segment of the secondary structure forming region wherein the blocking sequence disrupts formation of the unwanted secondary structure in an amplicon thereby enabling detection and amplification of the site of interest" is functional language which imparts no structural limitations to the claimed primer. See ***Claim Interpretation*** above).

With regard to claim 2, Wilton et al. teach the site of interest is a nucleic acid sequence (see p. 253 col. 2 under Polymerase Chain Reaction, where the target is mouse DNA).

With regard to claim 3, Wilton et al. teach the site of interest is a single nucleotide polymorphism (see p. 253 col. 1 second full paragraph and p. 254 Figure 1, where the snp is C to T *mdx* mutation).

With regard to claim 4, Wilton et al. teach the primer sequence is complementary to one terminus of the target molecule containing the target nucleotide sequence (see p. 254 Figure 1 and p. 253 Table 1).

With regard to claim 5, Wilton et al. teach further including a nonhybridizing spacer between the primer sequence and the blocking sequence (see p. 256, Figure 3 and legend, where the nonhybridizing sequence is the sequence which anneals back to the normal sequence therefore it does not hybridize with the target sequence carrying the mutation).

With regard to claim 9, Wilton et al. teach the spacer is nucleotidic (see p. 254 Figure 1 and p. 253 Table 1).

With regard to claim 12, Wilton et al. teach the spacer is an oligomeric segment comprised of a recurring single nucleotide (see p. 253 Table 1 SB-B(r) and SB-D(r), where the recurring single nucleotide is A).

With regard to claim 13, Wilton et al. teach the probe sequence and the spacer are separated from each other by a means for halting transcription there between (see p. 253 Table 1 where the primer sequence is separated from the snap back sequence by the nucleotide G, which meets the structural limitation recited in the claim because the recitation "by a means for halting transcription there between" is functional language).

With regard to claim 14, Wilton et al. teach the means for halting transcription is an arresting linker (see p. 253 Table 1 where the primer sequence is separated from the snap back sequence by the nucleotide G, which meets the structural limitation recited in the claim because the recitation "an arresting linker" is functional language).

With regard to claim 26, Wilton et al. teach an amplicon formed by the action of a DNA polymerase on the primer of claim 1 hybridized to the target nucleotide sequence (see p 253 under polymerase chain reaction and Figure 1 and legend).

Claims 1, 2 and 4-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Bannwarth et al. (USPN 5,573,906, 1996).

With regard to claim 1, Bannwarth et al. teach a dual-purpose primer for amplifying a target nucleotide sequence in a target molecule, wherein the target nucleotide sequence contains a site of interest proximal to or contained within a secondary structure forming region that, in the absence of the primer, results in an unwanted secondary structure in an amplicon formed under amplification conditions so as to prevent detection of the site of interest, wherein the primer comprises:

(a) a primer sequence complementary to a segment of the target nucleotide sequence other than the secondary structure forming region (see col. 2 lines 17-34 and Figure 1, where Bannwarth et al. clearly teach a primer sequence which is complementary to a target nucleotide sequence which is the only structural limitation recited. See ***Claim Interpretation*** above); and

(b) a blocking sequence substantially complementary to a segment of the secondary structure forming region wherein the blocking sequence disrupts formation of the unwanted secondary structure in an amplicon thereby enabling detection and amplification of the site of interest (see col. 2 lines 17-34 and Figure 1, where Bannwarth et al. clearly teach a primer sequence which is complementary to a target nucleotide sequence which is the only structural limitation recited. The recitation of "blocking sequence substantially complementary to a segment of the secondary structure forming region wherein the blocking sequence disrupts formation of the unwanted secondary structure in an amplicon thereby enabling detection and amplification of the site of interest" is functional language which imparts no structural limitations to the nucleic acid. See ***Claim Interpretation*** above).

With regard to claim 2, Bannwarth et al. teach the site of interest is a nucleic acid sequence (see col. 2 lines 21-23).

With regard to claim 4, Bannwarth et al. teach the primer sequence is complementary to one terminus of the target molecule containing the target nucleotide sequence (see Figure 1 and col. 2 lines 17-34).

With regard to claim 5, Bannwarth et al. teach further including a nonhybridizing spacer between the primer sequence and the blocking sequence (see col.2 lines 25-34, where the nonhybridizing sequence is the linker).

With regard to claim 6, Bannwarth teach the spacer is non-nucleotidic (see col. 2 lines 25-34).

With regard to claim 7, Bannwarth teach the spacer is comprised of a synthetic hydrophilic oligomer (see col. 6 lines36-52, where the linker is comprised of two propanediol groups linker by a phosphate, making it hydrophilic).

Claims 1 and 5-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Laibinis et al. (US 2002/0028455, March 2002).

With regard to claim 1, Laibinis et al. teach a dual-purpose primer for amplifying a target nucleotide sequence in a target molecule, wherein the target nucleotide sequence contains a site of interest proximal to or contained within a secondary structure forming region that, in the absence of the primer, results in an unwanted secondary structure in an amplicon formed under amplification conditions so as to prevent detection of the site of interest, wherein the primer comprises:

(a) a primer sequence complementary to a segment of the target nucleotide sequence other than the secondary structure forming region (see paragraphs 0010, 0040 and 0041, where Laibinis et al. clearly teach a nucleotide sequence which is complementary to a target nucleotide sequence and which has a 3' extendable end which are the only structural limitations recited. See ***Claim Interpretation*** above); and

(b) a blocking sequence substantially complementary to a segment of the secondary structure forming region wherein the blocking sequence disrupts formation of the unwanted secondary structure in an amplicon thereby enabling detection and amplification of the site of interest (see paragraphs 0010, 0040 and 0041, where Laibinis et al. clearly teach a nucleotide sequence which is complementary to a target nucleotide sequence and which has a 3' extendable end which are the only structural limitations recited. The recitation of "blocking sequence substantially complementary to a segment of the secondary structure forming region wherein the blocking sequence disrupts formation of the unwanted secondary structure in an amplicon thereby enabling detection and amplification of the site of interest" is functional language which imparts no structural limitations to the nucleic acid. See ***Claim Interpretation*** above).

With regard to claim 5, Laibinis et al. teach further including a nonhybridizing spacer between the primer sequence and the blocking sequence (see paragraph 0014, where the nonhybridizing sequence is the linking moiety).

With regard to claim 6, Laibinis teach the spacer is non-nucleotidic (see paragraph 0014).

With regard to claim 7, Laibinis teach the spacer is comprised of a synthetic hydrophilic oligomer (see paragraph 0014, where the linker is comprised of chains of alkylene units, specifically polyethylene glycol, making it hydrophilic).

With regard to claim 8, Laibinis teach the spacer is comprised of about 3 to about 50 alkylene oxide units selected from ethylene oxide and combinations of ethylene oxide and propylene oxide (see paragraph 0014).

Claims 1, 17, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Beattie et al. (USPN 6,268,147, 2001).

With regard to claim 1, Beattie et al. teach a dual-purpose primer for amplifying a target nucleotide sequence in a target molecule, wherein the target nucleotide sequence contains a site of interest proximal to or contained within a secondary structure forming region that, in the absence of the primer, results in an unwanted secondary structure in an amplicon formed under amplification conditions so as to prevent detection of the site of interest, wherein the primer comprises:

(a) a primer sequence complementary to a segment of the target nucleotide sequence other than the secondary structure forming region (see col. 20 lines 31-66, where Beattie et al. clearly teach a teach a nucleotide sequence which is complementary to a target nucleotide sequence and which has a 3' extendable end which are the only structural limitations recited. See ***Claim Interpretation*** above); and

(b) a blocking sequence substantially complementary to a segment of the secondary structure forming region wherein the blocking sequence disrupts formation of the unwanted secondary structure in an amplicon thereby enabling detection and amplification of the site of interest (see col. 20 lines 31-66, where Beattie et al. clearly teach a nucleotide sequence which is complementary to a target nucleotide sequence and which has a 3' extendable end which are the only structural limitations recited. The recitation of "blocking sequence substantially complementary to a segment of the secondary structure

forming region wherein the blocking sequence disrupts formation of the unwanted secondary structure in an amplicon thereby enabling detection and amplification of the site of interest" is functional language which imparts no structural limitations to the nucleic acid. See ***Claim Interpretation*** above).

With regard to claim 17, Beattie et al. teach further comprising a detectable label (see col. 20 lines 33-66 to col. 21 lines 1-37).

With regard to claim 18, Beattie et al. teach the detectable label is a radioactive isotope (see col. 20 lines 33-66 to col. 21 lines 1-37, where ^{32}P is the label).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 27-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilton et al. (Human Mutation 1998, cited in the IDS) in view of the Stratagene Catalog (1988).

With regard to claim 27, Wilton et al. teach a dual-purpose primer according to claim 1, nucleotides appropriate to amplification of an oligonucleotide sequence, and an agent for polymerization of the nucleotides (see p. 253 col. 2 under polymerase chain reaction).

With regard to claim 28, Wilton et al. teach a dual-purpose primer according to claim 1, a second primer, nucleotides appropriate to DNA amplification, an agent for polymerization of the nucleotides, an allele specific hybridization (ASH) probe having a nucleotide capture region, and color-coded detecting means having a nucleotide capture region complementary to the nucleotide capture region on said ASH probe, wherein the nucleotide capture region on said detecting means is complementary to said ASH

probe such that the target nucleotide sequence is identified by the color-coding of said detecting means (see p. 253 col. 2 under polymerase chain reaction and gel fractionation and detection of bands, where the recitation of kit is not given patentable weight and the recitation of "for determining the genotype of an individual" is an intended use recitation).

With regard to claim 29, Wilton et al. teach the detecting means is a multiplex detecting means (see p. 253 col. 2 under polymerase chain reaction and gel fractionation and detection of bands and Figure 1, where multiple alleles are detected).

With regard to claim 30, Wilton et al. teach the multiplex detecting means comprises a detectable solid substrate (see p. 253 col. 2 under polymerase chain reaction and gel fractionation and detection of bands and Figure 1, where multiple alleles are detected and the solid substrate is the polyacrylamide gel).

With regard to claim 32, Wilton et al. teach a hybridization probe comprising (a) a probe nucleotide sequence complementary to a first nucleotide sequence in a target molecule, and (b) a blocking sequence substantially complementary to a second nucleotide sequence in a target molecule, wherein hybridization of the blocking sequence with the second nucleotide sequence prevents secondary structure formation in the second nucleotide sequence that would otherwise interfere with hybridization of the probe sequence to the first nucleotide sequence (see p. 253, Table 1 and col. 2 lines 10-17 and Figure 1, where Wilton et al. clearly teach a primer sequence which is complementary to a target nucleotide sequence which is the only structural limitation recited. The recitation of "probe" and "blocking sequence and "wherein hybridization of the blocking sequence with the second nucleotide sequence prevents secondary structure formation in the second nucleotide sequence that would otherwise interfere with hybridization of the probe sequence to the first nucleotide sequence" is functional language and imparts no structural limitation on the nucleic acid).

Wilton et al. do not teach or suggest a kit.

Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the dual purpose primer for amplification as taught by Wilton et al. into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. Thus one need not purchase gram quantities of 10 different reagents, each of which is needed in only microgram amounts, when beginning a series of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually far more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, premixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2). The other service provided in a kit is quality control" (page 39, column 1).

Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bannwarth et al. (USPN 5,573,906, 1996) in view of the Stratagene Catalog (1988).

With regard to claim 28, Bannwarth et al. teach a dual-purpose primer according to claim 1, a second primer, nucleotides appropriate to DNA amplification, an agent for polymerization of the nucleotides, an allele specific hybridization (ASH) probe having a nucleotide capture region, and color-coded detecting means having a nucleotide capture region complementary to the nucleotide capture region on said ASH probe, wherein the nucleotide capture region on said detecting means is complementary to said ASH probe such that the target nucleotide sequence is identified by the color-coding of said detecting means (see col. 2 lines 17-44 and Figure 1, where Bannwarth et al. clearly teach a primer sequence which is complementary to a target nucleotide sequence which is the only structural limitation recited. The recitation of "blocking sequence substantially complementary to a segment of the

secondary structure forming region to prevent formation of the unwanted secondary structure" is functional language which imparts no structural limitations to the nucleic acid).

Bannwarth et al. do not teach or suggest a kit.

Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the dual purpose primer for amplification as taught by Wilton et al. into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. Thus one need not purchase gram quantities of 10 different reagents, each of which is needed in only microgram amounts, when beginning a series of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually far more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, premixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2). The other service provided in a kit is quality control" (page 39, column 1).

Claim 28-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beattie et al. (USPN 6,268,147, 2001) in view of the Stratagene Catalog (1988).

With regard to claim 28, Beattie et al. teach a dual-purpose primer according to claim 1, a second primer, nucleotides appropriate to DNA amplification, an agent for polymerization of the nucleotides, an allele specific hybridization (ASH) probe having a nucleotide capture region, and color-coded detecting means having a nucleotide capture region complementary to the nucleotide capture region on said ASH probe, wherein the nucleotide capture region on said detecting means is complementary to said ASH

probe such that the target nucleotide sequence is identified by the color-coding of said detecting means (see example 10, where Beattie et al. clearly teach a primer sequence which is complementary to a target nucleotide sequence which is the only structural limitation recited. The recitation of "blocking sequence substantially complementary to a segment of the secondary structure forming region to prevent formation of the unwanted secondary structure" is functional language which imparts no structural limitations to the nucleic acid.).

With regard to claim 29, Beattie et al. teach the detecting means is a multiplex detecting means (see example 10, where multiple alleles are detected).

With regard to claim 30, Beattie et al. teach the multiplex detecting means comprises a detectable solid substrate (see example 10, where multiple alleles are detected and the solid substrate is the glass substrate for the array, or any of the substrates recited in lines 11-14 of col. 30).

With regard to claim 31, Beattie et al. teach the detectable solid substrate is a detectable microsphere (see col. 40 lines 19-28 and Figure 15 A and B).

With regard to claim 32, Beattie et al. teach a hybridization probe comprising (a) a probe nucleotide sequence complementary to a first nucleotide sequence in a target molecule, and (b) a blocking sequence substantially complementary to a second nucleotide sequence in a target molecule, wherein hybridization of the blocking sequence with the second nucleotide sequence prevents secondary structure formation in the second nucleotide sequence that would otherwise interfere with hybridization of the probe sequence to the first nucleotide sequence (see col. 20 lines 31-66, where Beattie et al. clearly teach a probe sequence which is complementary to a target nucleotide sequence which is the only structural limitation recited. The recitation of "probe" and "blocking sequence and "wherein hybridization of the blocking sequence with the second nucleotide sequence prevents secondary structure formation in the second nucleotide sequence that would otherwise interfere with hybridization of the probe sequence to the first nucleotide sequence" is functional language and imparts no structural limitation on the nucleic acid).

With regard to claim 33, Beattie et al. teach further comprising a detectable label (see col. 20 lines 33-66 to col. 21 lines 1-37).

With regard to claim 34, Beattie et al. teach the detectable label is a radioactive labels (see col. 20 lines 33-66 to col. 21 lines 1-37, where ^{32}P is the label).

Beattie et al. do not teach or suggest a kit.

Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the dual purpose primer for amplification as taught by Wilton et al. into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. Thus one need not purchase gram quantities of 10 different reagents, each of which is needed in only microgram amounts, when beginning a series of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually far more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, premixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2). The other service provided in a kit is quality control" (page 39, column 1).

Claims 10, 11, 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilton et al. (Human Mutation 1998) in view of Fisher (USPN 6,054,568, 2000).

The teachings of Wilton et al. are described previously.

Wilton et al. do not teach all of the limitations of claims 10, 11, 15 and 16.

With regard to claim 10, Fisher teaches the use of a non-natural base in a primer (see col. 8 lines 4-22).

With regard to claims 11, 15 and 16, Fisher teaches iso-cytosine and iso-guanine (see col. 8 lines 4-22, where iso-cytosine and iso-guanine are modified nucleosides)

One of ordinary skill in the art at the time the invention was made would have been motivated to use the non natural bases as taught by Fisher with the primer as taught by Wilton in order to improve properties such as affinity and specificity of hybridization to complementary nucleic acids. Wilton teaches the presence of the non natural base will increase specificity and affinity with respect to hybridization to complementary nucleic acids (see col. 8 lines 4-22). An ordinary practitioner would have been motivated to use the non natural bases as taught by Fisher with the primer as taught by Wilton in order to improve affinity and specificity of hybridization of the primer in the PCR reactions used to assess the presence of single nucleotide polymorphisms.

(10) Response to Argument

The Claim Interpretation is Factually and Legally Correct

Appellants assert the position of the Office with respect to the recitation of the blocking sequence is that it is described with functional language warranting no patentable weight. This is not a correct characterization of the position of the Office with respect to the blocking sequence recitation. The Office states that, "As written, the claimed primer is anticipated by any prior art primer for which a target sequence exists **or could be synthesized** such that the functional limitations and intended uses recited in the claims are fulfilled." Here the Office clearly acknowledges the functional limitations and intended use recitations must be fulfilled, but in this case these recitations are inherent features of each of the prior art primers. The rejections made of record in the Office Action mailed December 28, 2007, consider the functional limitations and intended uses recited in the instant claims, however it is the position of the

Office that the "blocking sequence" as claimed is an inherent feature of each of the prior primers, and therefore the functional language and intended use recitation is necessarily fulfilled.

Appellants argue the recitation of the blocking sequence is not properly addressed as a structural limitation. This argument is not correct. The recitation in claim 1 of b) states, "a blocking sequence substantially complementary to a segment of *the secondary structure forming region*, wherein the blocking sequence disrupts formation of the *unwanted secondary structure in an amplicon* thereby enabling detection and amplification of the site of interest." The phrases *the secondary structure forming region* and *unwanted secondary structure in an amplicon* refer back to the target DNA not the primer. The recited secondary structure is in the ***target*** not the ***primer*** and Appellants are claiming the ***prime***r not the ***target***. Therefore the blocking sequence is an inherent feature of the prior art primers. Appellants argue the office asserts the blocking sequence is strictly a functional recitation. This is correct. The blocking sequence is not specifically defined in such a way as to distinguish it from any other nucleotide sequence within the primer. For example the blocking sequence contains no specific polynucleotide sequence nor does the sequence correspond to a specific template sequence, but rather it is defined by its function, specifically, the blocking is substantially complementary to a segment of the secondary structure forming region, wherein the blocking sequence disrupts formation of the unwanted secondary structure in an amplicon thereby enabling detection and amplification of the site of interest. For all of these reasons the claim interpretation is factually and legally correct.

Written Description

Appellants argue the written description rejection is improper because it stems from improper interpretation of the claims. Appellants argue each of the Federal Circuit cases are not relevant because they relate to new species of nucleic acids and/or proteins, and the instant claims are drawn to a general purpose primer. This argument is not persuasive because all primers are nucleic acids and therefore the

case law is relevant. All of the instant claims are directed to isolated polynucleotides of one form or another which are complementary to, or substantially complementary to, or capable of being extended on an unspecified target sequence. Appellants specify no particular sequence for either the target or the primer, which creates an incredibly large genus of potential polynucleotides covered by the claims. The claims encompass any polynucleotide for which a target sequence exists *or could be synthesized.*

The fact patterns of each of the recited Federal Circuit cases are analogous to the instant claims as discussed at length in the rejection supra. Appellants point to no specific legal defect in the written description rejection but rather espouse the attributes of the instantly claimed primers. Additionally, Appellants fail to provide any meaningful argument with respect to representative number of species. Therefore the arguments are not found to be persuasive and the rejection is properly made and should be maintained.

Claims 1-5, 9, 12-14 and 26 are anticipated by Wilton et al.

With respect to claims 1-4 and 26, Appellants argue the structural nature of clause b) of instant claim 1. These arguments are not persuasive because claim 1 recites, "A dual purpose primer *for amplifying a target nucleotide sequence in a target molecule*, ***wherein the target molecule has a secondary structure forming region and further wherein the target nucleotide sequence contains a site of interest proximal to or contained within the secondary structure forming region***, wherein the primer comprises; (a) a primer sequence complementary to a segment of the target nucleotide sequence other than ***the secondary structure forming region***; and (b) a blocking sequence substantially complementary ***to a segment of the secondary structure forming region, wherein the blocking sequence disrupts formation of the unwanted secondary structure in an amplicon thereby enabling detection and amplification of the site of interest.***

Appellants are claiming the primer not the target. The language which is in bold italics is directed to the target molecule in terms of structure and function. The language which is in italics only is intended use language. Wilton et al. meet all of the structural limitations of clause (a) and inherently meets all of the functional limitations for clause (b), as well as the intended use recitation in italics. Wilton's primer A(f) in Table 1 will inherently meet the functional limitations of clause (b) when an appropriate target is present. Appellants are claiming only the primer, therefore the target does not need to be present in the prior art document. The inherency property of Wilton's primer is exemplified in the drawing below.

Target XXXXCGTTTCA TCCATAGGCTAA

Wilton's primer CTCTGCAAAGTTCTTTGAAAGAGTAA

The underlined blue nucleotides in Wilton's primer correspond to clause (a) a primer sequence complementary to a segment of the target nucleotide sequence other than the secondary structure forming region; The nucleotides in green italics correspond to the blocking sequence as functionally defined in clause (b) a blocking sequence substantially complementary to a segment of the secondary structure forming region, wherein the blocking sequence disrupts formation of the unwanted secondary structure in an amplicon thereby enabling detection and amplification of the site of interest. When the primer of Wilton hybridizes to the target the secondary structure of the target will be disrupted and the site in blue will be available for detection or amplification. Patentable weight was given to clause (b) and the primer

of Wilton inherently possesses the functional properties of clause (b) for this particular target. Therefore Wilton et al. anticipates instant claims 1-5, 9, 12-14 and 26.

Claims 1, 2 and 4-7 are anticipated by Bannwarth et al.

With respect to claims 1, 2 and 4-7, Appellants argue the structural nature of clause b) of instant claim 1. These arguments are not persuasive because claim 1 recites, "A dual purpose primer *for amplifying a target nucleotide sequence in a target molecule*, ***wherein the target molecule has a secondary structure forming region and further wherein the target nucleotide sequence contains a site of interest proximal to or contained within the secondary structure forming region***, wherein the primer comprises; (a) a primer sequence complementary to a segment of the target nucleotide sequence other than ***the secondary structure forming region***; and (b) a blocking sequence substantially complementary ***to a segment of the secondary structure forming region, wherein the blocking sequence disrupts formation of the unwanted secondary structure in an amplicon thereby enabling detection and amplification of the site of interest.***

Appellants are claiming the primer not the target. The language which is in bold italics is directed to the target molecule in terms of structure and function. The language which is in italics only is intended use language. Bannwarth et al. meet all of the structural limitations of clause (a) and inherently meets all of the functional limitations for clause (b), as well as the intended use recitation in italics. Bannwarth's primer, col. 11 line 49 (SEQ ID NO: 2, primer 15) will inherently meet the functional limitations of clause (b) when an appropriate target is present. Appellants are claiming only the primer, therefore the target does not need to be present in the prior art document. The inherency property of Bannwarth's primer is exemplified in the drawing below.

	CG TA CG CG TA AT CG TA GC
Target	ATAGG CTAGGTAAGCC
Bannwarth's primer 15	TATCCCAGTAGGAGAAAT

The underlined blue nucleotides in Bannwarth's primer correspond to clause (a) a primer sequence complementary to a segment of the target nucleotide sequence other than the secondary structure forming region; The nucleotides in green italics correspond to the blocking sequence as functionally defined in clause (b) a blocking sequence substantially complementary to a segment of the secondary structure forming region, wherein the blocking sequence disrupts formation of the unwanted secondary structure in an amplicon thereby enabling detection and amplification of the site of interest. When the primer of Bannwarth hybridizes to the target the secondary structure of the target will be disrupted and the site in blue will be available for detection or amplification. Patentable weight was given to clause (b) and the primer of Bannwarth inherently possesses the functional properties of clause (b) for this particular target. Therefore Bannwarth et al. anticipates instant claims 1, 2 and 4-7.

Claims 1 and 5-8 are anticipated by Laibinis et al.

With respect to claims 1 and 5-8, Appellants argue the structural nature of clause b) of instant claim 1. These arguments are not persuasive because claim 1 recites, "A dual purpose primer *for amplifying a target nucleotide sequence in a target molecule*, ***wherein the target molecule has a secondary structure forming region and further wherein the target nucleotide sequence contains a site of interest proximal to or contained within the secondary structure forming region***, wherein the primer

comprises; (a) a primer sequence complementary to a segment of the target nucleotide sequence other than ***the secondary structure forming region***; and (b) a blocking sequence substantially complementary ***to a segment of the secondary structure forming region, wherein the blocking sequence disrupts formation of the unwanted secondary structure in an amplicon thereby enabling detection and amplification of the site of interest.***

Appellants are claiming the primer not the target. The language which is in bold italics is directed to the target molecule in terms of structure and function. The language which is in italics only is intended use language. Laibinis et al. meet all of the structural limitations of clause (a) and inherently meets all of the functional limitations for clause (b), as well as the intended use recitation in italics. Laibinis et al. teach polynucleotides equal to about 100 bases and Laibinis et al. teach PCR primers at paragraph 0064. A PCR primer necessarily has a sequence complementary to a segment of a target nucleotide and while Laibinis et al. do not teach a specific sequence, any primer of Laibinis will inherently meet the functional limitations of clause (b) when an appropriate target is present. Appellants are claiming only the primer, therefore the target does not need to be present in the prior art document. Patentable weight was given to clause (b) and any primer of Laibinis inherently possesses the functional properties of clause (b) for this particular target. Therefore Laibinis et al. anticipates instant claims 1 and 5-8.

Claims 1 and 17-18 are anticipated by Beattie et al.

With respect to claims 1 and 17-18, Appellants argue the structural nature of clause b) of instant claim 1. These arguments are not persuasive because claim 1 recites, "A dual purpose primer *for amplifying a target nucleotide sequence in a target molecule*, ***wherein the target molecule has a secondary structure forming region and further wherein the target nucleotide sequence contains a site of interest proximal to or contained within the secondary structure forming region***, wherein the primer comprises; (a) a primer sequence complementary to a segment of the target nucleotide sequence other

than ***the secondary structure forming region***; and (b) a blocking sequence substantially complementary ***to a segment of the secondary structure forming region, wherein the blocking sequence disrupts formation of the unwanted secondary structure in an amplicon thereby enabling detection and amplification of the site of interest.***

Appellants are claiming the primer not the target. The language which is in bold italics is directed to the target molecule in terms of structure and function. The language which is in italics only is intended use language. Bannwarth et al. meet all of the structural limitations of clause (a) and inherently meets all of the functional limitations for clause (b), as well as the intended use recitation in italics. Beattie's primer, col. 20 line 14 (SEQ ID NO: 2) will inherently meet the functional limitations of clause (b) when an appropriate target is present. Appellants are claiming only the primer, therefore the target does not need to be present in the prior art document. The inherency property of Beattie's primer is exemplified in the drawing below.

Target XXXGTCACC TCGTTAAGAG

Beattie's primer GCACAGTGGAAGAATTCATTCTG

The underlined blue nucleotides in Beattie's primer correspond to clause (a) a primer sequence complementary to a segment of the target nucleotide sequence other than the secondary structure forming region; The nucleotides in green italics correspond to the blocking sequence as functionally defined in clause (b) a blocking sequence substantially complementary to a segment of the secondary structure forming region, wherein the blocking sequence disrupts formation of the unwanted secondary structure in

an amplicon thereby enabling detection and amplification of the site of interest. When the primer of Beattie hybridizes to the target the secondary structure of the target will be disrupted and the site in blue will be available for detection or amplification. Patentable weight was given to clause (b) and the primer of Beattie inherently possesses the functional properties of clause (b) for this particular target. Therefore Beattie et al. anticipates instant claims 1 and 17-18.

All rejections made under 35 USC 103 (a) stand.

Appellants argue with respect to all 103 (a) rejections that the secondary reference cannot cure the failure of each of the primary references to teach the claimed dual purpose primer. These arguments are not persuasive because as argued supra each of the cited primary references *does* teach the claimed dual-purpose primer.

The Claim Term "Substantially complementary" is proper.

This term is not germane to the rejections at issue or to the claim interpretation, as acknowledged by Appellant in the second full sentence of the first paragraph under **K.** on p.29 of the instant brief. Therefore comments made by Appellant regarding this language will not be addressed. It is the opinion of the Office that comments made by Appellants with respect to this language have no bearing on the substance of the rejections currently before the board.

(11) Related Proceeding(s) Appendix

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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